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FILE COVERS 1907 - 26 Apr 2004 VOL 140 ISS 18
FILE LAST UPDATED: 25 Apr 2004 (20040425/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

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=> s ((keratinocyte (w)growth(w) factor) or KGF(2w)2) and inflam?
         10992 KERATINOCYTE
         10741 KERATINOCYTES
         13809 KERATINOCYTE
                 (KERATINOCYTE OR KERATINOCYTES)
       1114750 GROWTH
          4062 GROWTHS
       1116846 GROWTH
                 (GROWTH OR GROWTHS)
        828369 FACTOR
        731088 FACTORS
       1309510 FACTOR
                 (FACTOR OR FACTORS)
           813 KERATINOCYTE (W)GROWTH(W) FACTOR
          2850 KGF
             3 KGFS
          2850 KGF
                 (KGF OR KGFS)
       8024309 2
           167 KGF(2W)2
        181839 INFLAM?
L5         109 ((KERATINOCYTE (W)GROWTH(W) FACTOR) OR KGF(2W)2) AND INFLAM?

=> s (((keratinocyte (w)growth(w) factor)(2w)2) or KGF(2w)2) and inflam?
         10992 KERATINOCYTE
         10741 KERATINOCYTES
         13809 KERATINOCYTE
                 (KERATINOCYTE OR KERATINOCYTES)
       1114750 GROWTH
          4062 GROWTHS
       1116846 GROWTH
                 (GROWTH OR GROWTHS)
        828369 FACTOR
        731088 FACTORS
       1309510 FACTOR
                 (FACTOR OR FACTORS)
       8024309 2
            50 (KERATINOCYTE (W)GROWTH(W) FACTOR)(2W)2
          2850 KGF
             3 KGFS
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          2850 KGF
                 (KGF OR KGFS)
       8024309 2
           167 KGF(2W)2
        181839 INFLAM?
L6          19 (((KERATINOCYTE (W)GROWTH(W) FACTOR)(2W)2) OR KGF(2W)2) AND
               INFLAM?

=> d bib,abs 1-19

L6   ANSWER 1 OF 19  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:132265  CAPLUS
DN   140:157940
TI   Characterization, production and therapeutic uses of keratinocyte
     growth factor-2 (KGF-2)
     fragments and analogs
IN   Ruben, Steven M.; Jimenez, Pablo; Duan, D. Roxanne; Rampy, Mark A.;
     Mendrick, Donna; Zhang, Jun; Ni, Jian; Moore, Paul A.; Coleman, Timothy
     A.; Gruber, Joachim R.; Dillon, Patrick J.; Gentz, Reiner L.
PA   Human Genome Sciences, Inc., USA
SO   U.S., 244 pp., Cont.-in-part of U.S. Ser. No. 345,373.
     CODEN: USXXAM
DT   Patent
LA   English
FAN.CNT 5
     PATENT NO.         KIND  DATE          APPLICATION NO.   DATE
     ----------------   ----  --------      ---------------   --------
PI   US 6693077         B1    20040217      US 2000-610651    20000630
     CA 2430223         AA    19960822      CA 1995-2430223   19950214
     WO 9625422         A1    19960822      WO 1995-US1790    19950214
         W:  AU, CA, CN, JP, KR, MX, NZ, US
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
     EP 1323824         A2    20030702      EP 2003-6708      19950214
     EP 1323824         A3    20040121
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE
     PT 815115          T     20031031      PT 1995-911700    19950214
     ES 2194049         T3    20031116      ES 1995-911700    19950214
     EP 1247530         A2    20021009      EP 2002-1059      19970813
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     EP 1247862         A2    20021009      EP 2002-1060      19970813
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     US 6077692         A     20000620      US 1998-23082     19980213
     US 2003077695      A1    20030424      US 1999-345373    19990701
     JP 2003520572      T2    20030708      JP 2001-508220    20000703
     NZ 516897          A     20040130      NZ 2000-516897    20000703
PRAI WO 1995-US1790     A2    19950214
     US 1995-461195     A3    19950605
     US 1996-23852P     P     19960813
     US 1996-696135     A2    19960813
     US 1997-39045P     P     19970228
     US 1997-862432     A2    19970523
     US 1997-55561P     P     19970813
     US 1997-910875     A2    19970813
     US 1998-23082      A1    19980213
     US 1999-345373     A2    19990701
     US 1999-142343P    P     19990702
     US 1999-143648P    P     19990714
     US 1999-144024P    P     19990715
     US 1999-148628P    P     19990812
     US 1999-149935P    P     19990819
     US 1999-163375P    P     19991103
     US 1999-171677P    P     19991222
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US 2000-198322P P 20000419
US 2000-205417P P 20000519
CA 1995-2210444 A3 19950214
EP 1995-911700 A3 19950214
EP 1997-937200 A3 19970813
US 2000-610651 A 20000630
WO 2000-US18328 W 20000703

AB This invention relates to newly identified polynucleotides, polypeptides encoded by such polynucleotides, the use of such polynucleotides and polypeptides, as well as the production of such polynucleotides and polypeptides. More particularly, the polypeptide of the present invention is a Keratinocyte Growth Factor, sometimes hereinafter referred to as "**KGF-2**". This invention further relates to the therapeutic use of **KGF-2** to promote or accelerate wound healing. This invention also relates to novel mutant forms of **KGF-2** that show enhanced activity, increased stability, higher yield or better solubility

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:1007590 CAPLUS
DN 140:47549
TI Amniotic membrane-mediated delivery of bioactive molecules
IN Zhang, Fen
PA USA
SO U.S. Pat. Appl. Publ., 28 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003235580	A1	20031225	US 2003-603385	20030624
PRAI US 2002-391550P	P	20020624		

AB The present invention provides reconstituted and recombinant tissue membranes and methods for pharmaceutical delivery of bioactive mols. In particular, reconstituted and recombinant amniotic membranes are provided for sustained delivery of therapeutic mols., proteins or metabolites, to a site of a host in need thereof. The reconstituted and recombinant amniotic membrane contains one or more recombinant expression vectors that are exogenous to the membrane and capable of expressing bioactive mols. The reconstituted and recombinant tissue membranes and methods can be used for in situ delivery of therapeutic proteins to a host in the treatment of disorders such as chronic wounds and dermatol. or ocular surface diseases. For example, growth factor PDGF-β, delivered by prototypic reconstituted amniotic membrane, promoted healing of ischemic wounds on rabbit ears as a model of the ischemic conditions of human chronic wounds.

L6 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:574127 CAPLUS
DN 139:208226
TI Repifermin (**keratinocyte growth factor-2**) for the treatment of active ulcerative colitis: a randomized, double-blind, placebo-controlled, dose-escalation trial
AU Sandborn, W. J.; Sands, B. E.; Wolf, D. C.; Valentine, J. F.; Safdi, M.; Katz, S.; Isaacs, K. L.; Wruble, L. D.; Katz, J.; Present, D. H.; Loftus, E. V., Jr.; Graeme-Cook, F.; Odenheimer, D. J.; Hanauer, S. B.
CS Mayo Clinic, Rochester, MN, USA
SO Alimentary Pharmacology and Therapeutics (2003), 17(11), 1355-1364
CODEN: APTHEN; ISSN: 0269-2813
PB Blackwell Publishing Ltd.
DT Journal
LA English

AB Background: Repifermin (**keratinocyte growth factor-2**) has been shown to reduce **inflammation** in animal models of colitis. Aim: To evaluate repifermin for the treatment of active ulcerative colitis. Methods: Eighty-eight patients with active ulcerative colitis were enrolled in a 6-wk, double-blind trial. Patients were randomized to receive treatment for five consecutive days with i.v. repifermin at a dose of 1, 5, 10, 25 or 50 μg/kg, or placebo. The primary objective of the study was to evaluate the safety of repifermin. The primary efficacy outcome was clin. remission at week 4, defined as a score of zero on the endoscopic appearance and stool blood components of the Mayo score and a score of zero or unity on the stool frequency and physician's global assessment components. Results: At week 4, the rates of clin. remission in the 1, 5, 10, 25 and 50 μg/kg repifermin groups were 19%, 9%, 0%, 0% and 0%, resp., and 11% for the placebo group (P = 0.32 for repifermin vs. placebo). The frequencies of commonly occurring adverse events and severe adverse events were similar in both groups. Conclusions: I.v. repifermin at a dose of 1-50 μg/kg was very well tolerated, but there was no evidence that repifermin was effective for the treatment of active ulcerative colitis at these doses. An addnl. study to determine the efficacy of repifermin at doses of > 50 μg/kg or for a longer treatment duration may be warranted, as the maximally tolerated dose was not reached in the present study.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:116229 CAPLUS
DN 138:349019
TI Efficacy of repifermin (**keratinocyte growth factor-2**) against abnormalities in gastrointestinal mucosal transport in a murine model of colitis
AU Greenwood-Van Meerveld, B.; Venkova, K.; Connolly, K.
CS Basic Science Laboratories, Veterans Administration Medical Center, Oklahoma Foundation for Digestive Research, Oklahoma City, OK, 73104, USA
SO Journal of Pharmacy and Pharmacology (2002), Volume Date 2003, 55(1), 67-75
CODEN: JPPMAB; ISSN: 0022-3573
PB Pharmaceutical Press
DT Journal
LA English
AB Human **keratinocyte growth factor-2** (**KGF-2**) is a member of the fibroblast growth factor family that promotes healing of exptl. small intestinal ulceration and colitis. The aim of this study was to determine whether repifermin, a truncated form of recombinant human **KGF-2**, reverses abnormalities in colonic mucosal transport in a murine model of dextran sulfate sodium (DSS)-induced colitis. Male Swiss-Webster mice were given 4% DSS in drinking water for 7 days and then normal drinking water for 3 days. Repifermin (5 mg kg-1, i.p.) or vehicle was administered daily for 7 days starting on Day 4 of DSS exposure. On Day 10, net ion transport was measured electrophysiol. in colonic mucosal sheets. Repifermin significantly reduced DSS-induced colonic **inflammation** measured by tissue myeloperoxidase activity. Concurrently, in colonic tissue taken from mice treated with repifermin, there was a normalization of basal p.d. and short circuit current, and an improvement in the secretory responses to stimulation of muscarinic and ganglionic cholinoceptors. In control mice, repifermin did not interact directly with colonic epithelial cells or intramural neurons to induce immediate changes in net electrogenic transport. The results suggest that repifermin therapy may improve the mucosal electrogenic transport that is impaired during colitis.

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:754522 CAPLUS
DN 137:273196
TI Use of human **keratinocyte growth factor 2** to treat **inflammation**, stimulate growth of pulmonary epithelium, and prevent mucositis
IN Ruben, Steven M.; Jimenez, Pablo; Duan, D. Roxanne; Rampy, Mark A.; Mendrick, Donna; Zhang, Jun; Ni, Jian; Moore, Paul A.; Coleman, Timothy A.; Gruber, Joachim R.; Dillon, Patrick J.; Gentz, Reiner L.
PA Human Genome Sciences, Inc., USA
SO PCT Int. Appl., 583 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002077155	A2	20021003	WO 2002-US101	20020104
	WO 2002077155	A3	20030103		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003186904	A1	20031002	US 2002-35212	20020104
	EP 1357931	A2	20031105	EP 2002-736471	20020104
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	US 2001-259853P	P	20010108		
	US 2001-286368P	P	20010426		
	US 2001-331168P	P	20011109		
	WO 2002-US101	W	20020104		

AB N-terminal truncation mutants of **keratinocyte growth factor 2** (**KGF-2**), formerly known as fibroblast growth factor 12, may be used to treat **inflammation**, stimulate growth of pulmonary epithelium, and prevent mucositis. These truncated forms of **KGF-2** have enhanced activity, increased stability, higher yield, or better solubility Thus, cDNAs for mature **KGF-2**, **KGF-2**Δ28, and **KGF-2**Δ33 were expressed in Escherichia coli. **KGF-2**, **KGF-2**Δ28, and **KGF-2**Δ33 all strongly stimulated proliferation of BaF3 cells expressing the KGF receptor FGFR2IIIb isoform. The N-terminally truncated **KGF-2**Δ33 stimulated proliferation BaF3 cells better than the full-length KGF. **KGF-2**Δ33 stimulated wound healing in rats. In the PAF-induced paw edema **inflammation** model, **KGF-2**Δ33 exhibited anti-**inflammatory** effects. The survival rate of mice subjected to total body irradiation was improved when **KGF-2** Δ33 was administered before and after irradiation Intratracheal injection of **KGF-2**Δ33 resulted in increased proliferation of rat lung epithelial cells.

L6 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:657388 CAPLUS
DN 138:117892
TI In vitro and in vivo effects of repifermin (**keratinocyte growth factor-2**, **KGF-2**) on human carcinoma cells
AU Alderson, Ralph; Gohari-Fritsch, Shiva; Olsen, Hendrik; Roschke, Viktor;

Vance, Courtney; Connolly, Kevin
CS Human Genome Sciences, Inc., Rockville, MD, 20850, USA
SO Cancer Chemotherapy and Pharmacology (2002), 50(3), 202-212
CODEN: CCPHDZ; ISSN: 0344-5704
PB Springer-Verlag
DT Journal
LA English
AB Repifermin (**keratinocyte growth factor-2, KGF-2**) is a growth factor that selectively induces epithelial cell proliferation, differentiation and migration. The objective of this study was to assess the effect of repifermin on in vitro tumor cell proliferation and in vivo tumor growth using a variety of human carcinoma cell lines with differing growth rates and levels of KGF receptor (KGFR) expression. Potential effects of repifermin on in vitro cell proliferation were evaluated by alamarBlue and/or [3H]-thymidine incorporation assays under a range of serum conditions. In vivo tumor growth was evaluated by implanting KGFR+ carcinomas s.c. into nude mice and measuring tumor growth over time in mice injected i.v. or i.p. with repifermin or placebo. In vitro, none of the 30 human carcinoma cell lines tested demonstrated a substantial increase in proliferation in response to repifermin over the concentration range 0.01 to 1000 ng/mL. In vivo results showed no significant tumor growth-promoting activity when single- or multiple-cycle i.v. injections of repifermin (1 mg/kg) were given to athymic nude mice inoculated with human KGFR+ tumors of the pharynx (Detroit 562, FaDu), colon (Caco-2), salivary gland (A-253) or tongue (SCC-25, CAL 27). In addition, repifermin (0.2 or 2 mg/kg) injected i.p. for 2 wk had no effect on the growth of eight other human carcinomas including those of the ovary (NIH:OVCAR-3, SK-OV 3, PA-1), bladder (SCaBER), epidermis (A 431), lung (SW 900), breast (MDA-MB-231) and cervix (SiHa). Thus, repifermin had no in vitro or in vivo proliferative effects on KGFR+ human epithelial-like tumors. This failure to stimulate tumor cell growth highlights the ability of repifermin to specifically target normal epithelial tissue. This is critical to the safety profile of repifermin, since it is currently in phase II clin. trials for the treatment of cancer patients with mucositis resulting from chemo- or radiotherapy.
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:524730 CAPLUS
DN 137:304104
TI Biologic therapy of **inflammatory** bowel disease
AU Sandborn, William J.; Targan, Stephan R.
CS Inflammatory Bowel Disease Clinic, Division of Gastroenterology and Hepatology, Mayo Clinic and Mayo Foundation, Rochester, MN, USA
SO Gastroenterology (2002), 122(6), 1592-1608
CODEN: GASTAB; ISSN: 0016-5085
PB W. B. Saunders Co.
DT Journal; General Review
LA English
AB A review. Advancing knowledge regarding the biol. of chronic **inflammation** has led to the development of specific biol. therapies that mechanistically target individual **inflammatory** pathways. Many biol. therapies are being evaluated for the treatment of the chronic **inflammatory** bowel diseases, Crohn's disease and ulcerative colitis. Biol. compds. proven to be effective for Crohn's disease include monoclonal antibodies to tumor necrosis factor (infliximab and CDP571) and to the leukocyte adhesion mol. α4 integrin (natalizumab). Other biol. compds. for which there is insufficient evidence to judge efficacy for **inflammatory** bowel disease include: p55 tumor necrosis factor binding protein (onercept); interferon α; interferon β-1a; anti-interferon γ antibody; anti-interleukin 12 antibody; p65 anti-sense oligonucleotide (blocks

NF-κB); granulocyte colony stimulating factor, and granulocyte macrophage colony stimulating factor; anti-interleukin 2 receptor antibody; epidermal growth factor; **keratinocyte growth factor 2** (repifermin); human growth hormone; anti-CD4 antibody; and anti-α4β7 antibody. Biol. therapies that have been proven ineffective for **inflammatory** bowel disease include: interleukin 10; interleukin 11; antisense intercellular adhesion mol.-1; and the tumor necrosis factor receptor fusion protein etanercept. Based on the early successes of infliximab, CDP571 and natalizumab, it seems certain that biol. therapy will play an important role in the future treatment of **inflammatory** bowel disease.

RE.CNT 145 THERE ARE 145 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:439690 CAPLUS
DN 137:211281
TI Pharmacologic and pharmacokinetic profile of repifermin (**KGF-2**) in monkeys and comparative pharmacokinetics in humans
AU Sung, Cynthia; Parry, Tom J.; Riccobene, Todd A.; Mahoney, Angela; Roschke, Viktor; Murray, James; Gu, Mi Li; Glenn, Jeffrey K.; Caputo, Florence; Farman, Cindy; Odenheimer, Daniel J.
CS Human Genome Sciences, Inc., Rockville, MD, 20850, USA
SO PharmSci [online computer file] (2002), 4(2), No pp. given
CODEN: PHARFY; ISSN: 1522-1059
URL: http://www.pharmsci.org/scientificjournals/pharmsci/journal/040208.htm
PB American Association of Pharmaceutical Scientists
DT Journal; (online computer file)
LA English
AB Repifermin (truncated, recombinant human **keratinocyte growth factor-2**, **KGF-2**) was evaluated in cynomolgus monkeys and healthy humans during a phase 1 trial. Monkeys received vehicle or repifermin at 20, 75, or 200 μg/kg IV or 750 μg/kg s.c. (SC) daily for 29 days. Clin. observations were made during the entire dosing period. Gross and microscopic changes were assessed at necropsy. Pharmacokinetic parameters and immunogenicity were evaluated in these monkeys and in humans, following a single or 7 daily IV bolus injections of 1, 5, 25, or 50 μg/kg repifermin. In monkeys, repifermin was well tolerated, and histol. evaluation demonstrated dose-dependent, reversible thickening of the mucosa throughout the alimentary tract except for the stomach. In the alimentary tract tissues, nonepithelial tissues were not affected, indicating a specificity of repifermin for epithelial cells. Pharmacokinetics in both monkeys and humans were dose proportional, showed lack of drug accumulation with repeated daily dosing, and were characterized by high vols. of distribution and clearance rates, indicating substantial tissue binding and metabolism Repifermin was not markedly immunogenic following multiple daily IV injections in either species. Serum repifermin concns. in humans were comparable to those attained in monkeys that produced significant pharmacol. effects on epithelial cells in the alimentary tract. These findings provide addnl. support for the ongoing clin. development of repifermin for diseases involving epithelial injury.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:586258 CAPLUS
DN 135:339329
TI Repifermin (Human Genome Sciences/GlaxoSmithKline) glen wheeler
AU Anon.
CS Vancouver, BC, V5Z 1V1, Can.
SO IDrugs (2001), 4(7), 813-819
CODEN: IDRUFN; ISSN: 1369-7056

PB Current Drugs Ltd.
DT Journal; General Review
LA English
AB A review with refs. Human Genome Sciences (HGS) and GlaxoSmithKline (formerly SmithKline Beecham) are developing topical and injectable formulations of repifermin, **keratinocyte growth factor-2** (**KGF-2**), also known as fibroblast growth factor-10 (FGF-10) for the potential treatment of wound care, oral and intestinal mucositis, and **inflammatory** bowel diseases. A phase IIb trial of the topical formulation in chronic venous ulcers is ongoing, as well as phase II trials for the systemic, injectable formulation in ulcerative colitis and in the prevention of mucositis after chemotherapy with bone marrow transplantation. In May 2001, UBS Warburg predicted that HGS would receive approval of repifermin for the treatment of venous ulcers by year-end 2004, mucositis in 2005, and ulcerative colitis in the second half of 2004. In Oct. 2000, SmithKline Beecham exercised an option to codevelop repifermin for phase III trials and beyond. In May 2001, UBS Warburg valued repifermin's worldwide market at $2 billion for treating venous ulcers and predicted sales of $33 million in 2004 and $118 million in 2005 for this indication. In addition, the analysts regarded repifermin as having potential in the treatment of diabetic foot ulcers and pressure ulcers (a market valued at over $1.8 billion) and estimated that the drug might earn another $103.5 million for these indications in 2005. Furthermore, the analysts predicted sales of $6.8 million for repifermin's mucositis indication and, for ulcerative colitis, sales of $27.3 million in 2004 and $54.8 million in 2005. Overall, the analysts estimated that repifermin represented a $3.5 billion market opportunity for HGS/ GlaxoSmithKline and that commercialization of the drug might earn more than $61 million by 2004.
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:31534 CAPLUS
DN 134:95892
TI Cloning, cDNA sequence and biological activities of human **keratinocyte growth factor-2**
IN Ruben, Steven M.; Jimenez, Pablo; Duan, D. Roxannes; Rampy, Mark A.; Mendrick, Donna; Zhang, Jun; Ni, Jian; Moore, Paul A.; Coleman, Timothy A.; Gruber, Joachim R.; Dillon, Patrick J.; Gentz, Reiner L.
PA Human Genome Sciences, Inc., USA
SO PCT Int. Appl., 592 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001002433	A1	20010111	WO 2000-US18328	20000703
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2430223	AA	19960822	CA 1995-2430223	19950214
EP 1323824	A2	20030702	EP 2003-6708	19950214
EP 1323824	A3	20040121		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
PT 815115	T	20031031	PT 1995-911700	19950214
ES 2194049	T3	20031116	ES 1995-911700	19950214

EP 1196441 A1 20020417 EP 2000-945130 20000703
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
JP 2003520572 T2 20030708 JP 2001-508220 20000703
NZ 516897 A 20040130 NZ 2000-516897 20000703
PRAI US 1999-142343P P 19990702
US 1999-143648P P 19990714
US 1999-144024P P 19990715
US 1999-148628P P 19990812
US 1999-149935P P 19990819
US 1999-163375P P 19991103
US 1999-171677P P 19991222
US 2000-198322P P 20000419
US 2000-205417P P 20000519
CA 1995-2210444 A3 19950214
EP 1995-911700 A3 19950214
US 2000-610651 A 20000630
US 2000-610651P P 20000630
WO 2000-US18328 W 20000703

AB This invention relates to newly identified polynucleotides, polypeptides encoded by such polynucleotides, the use of such polynucleotides and polypeptides, as well as the production of such polynucleotides and polypeptides. More particularly, the polypeptide of the present invention is a keratinocyte growth factor, sometimes hereinafter referred to as "**KGF-2**" also formerly known as fibroblast growth factor 12 (FGF-12). **KGF-2** specifically stimulates growth of primary epidermal keratinocytes. Topical application of recombinant human **KGF-2** markedly accelerates the rate of healing of full-thickness excisional dermal wounds in diabetic mice. **KGF-2** shows significant activity in both glucocorticoid-impaired (methylprednisolone) and in normal excisional wound models. Thus, this invention further relates to the therapeutic use of **KGF-2** to promote or accelerate wound healing. This invention also relates to novel mutant forms of **KGF-2** that show enhanced activity, increased stability, higher yield, or better solubility

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:812953 CAPLUS
DN 134:13722
TI **Keratinocyte growth factor-2** (FGF-10) promotes healing of experimental small intestinal ulceration in rats
AU Han, Dong Soo; Li, Fengling; Holt, Lisa; Connolly, Kevin; Hubert, Melissa; Miceli, Renee; Okoye, Zebedee; Santiago, Gemma; Windle, Kathleen; Wong, Eling; Sartor, R. Balfour
CS Center for Gastrointestinal Biology and Disease, University of North Carolina, Chapel Hill, NC, 27599, USA
SO American Journal of Physiology (2000), 279(5, Pt. 1), G1011-G1022
CODEN: AJPHAP; ISSN: 0002-9513
PB American Physiological Society
DT Journal
LA English
AB **Keratinocyte growth factor-2** (**KGF-2**, repifermin) is a homolog of KGF-1 with epithelial mitogenic activities. We investigated the therapeutic role of **KGF-2** in intestinal ulceration and its mechanisms of protection. **KGF-2** (0.3-5 mg/kg) was administered before or after induction of small intestinal ulceration by indomethacin (Indo) in prevention and treatment protocols. In acute studies, **KGF-2** was injected for up to 7 days before or daily for 5 days after Indo. In a 15-day chronic study, **KGF-2** was injected i.v. daily beginning before or 7 days after Indo. Injury was evaluated by

blinded macroscopic and microscopic **inflammatory** scores, epithelial BrdU staining, tissue IL-1β, PGE2, and hydroxyproline concns., and collagen type I RNA expression. In vitro effects of **KGF-2** were evaluated by epithelial cellular proliferation, restitution of wounded monolayers, PGE2 secretion, and expression of COX-2 and collagen mRNA. The i.v. **KGF-2** significantly decreased acute intestinal injury by all parameters and significantly decreased chronic ulceration. Pretreatment, daily infusion, and delayed treatment were effective. **KGF-2** promoted in vitro epithelial restitution with only modest effects on epithelial cell proliferation, stimulated COX-2 expression in cultured epithelial cells, and upregulated in vitro and in vivo PGE2 production **KGF-2** did not affect in vivo fibrosis, although it induced collagen expression in cultured intestinal myofibroblasts. These results suggest that **KGF-2** inhibits intestinal **inflammation** by stimulating epithelial restitution and protective prostaglandins.

RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:415481 CAPLUS
DN 133:54115
TI Construction of deletion and substitution mutants of human **keratinocyte growth factor-2** and their use to promote wound healing
IN Ruben, Steven M.; Jimenez, Pablo; Duan, D. Roxanne; Rampy, Mark A.; Mendrick, Donna; Zhang, Jun; Ni, Jian; Moore, Paul A.; Coleman, Timothy A.; Gruber, Joachim R.; Dillon, Patrick J.; Gentz, Reiner L.
PA Human Genome Sciences, Inc., USA
SO U.S., 190 pp., Cont.-in-part of U.S. Ser. No. 910,875, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6077692	A	20000620	US 1998-23082	19980213
	CA 2430223	AA	19960822	CA 1995-2430223	19950214
	WO 9625422	A1	19960822	WO 1995-US1790	19950214
	W: AU, CA, CN, JP, KR, MX, NZ, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 1323824	A2	20030702	EP 2003-6708	19950214
	EP 1323824	A3	20040121		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	PT 815115	T	20031031	PT 1995-911700	19950214
	ES 2194049	T3	20031116	ES 1995-911700	19950214
	EP 1247530	A2	20021009	EP 2002-1059	19970813
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	EP 1247862	A2	20021009	EP 2002-1060	19970813
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 2003077695	A1	20030424	US 1999-345373	19990701
	US 6693077	B1	20040217	US 2000-610651	20000630
	US 2003129687	A1	20030710	US 2002-75446	20020215
PRAI	WO 1995-US1790	A2	19950214		
	US 1995-461195	B3	19950605		
	US 1996-23852P	P	19960813		
	US 1997-39045P	P	19970228		
	US 1997-862432	B2	19970523		
	US 1997-55561P	P	19970813		
	US 1997-910875	B2	19970813		
	CA 1995-2210444	A3	19950214		
	EP 1995-911700	A3	19950214		

US 1996-696135 A2 19960813
EP 1997-937200 A3 19970813
US 1998-23082 A1 19980213
US 1999-345373 A2 19990701
US 1999-142343P P 19990702
US 1999-143648P P 19990714
US 1999-144024P P 19990715
US 1999-148628P P 19990812
US 1999-149935P P 19990819
US 1999-163375P P 19991103
US 1999-171677P P 19991222
US 2000-198322P P 20000419
US 2000-205417P P 20000519

AB This invention relates to newly identified polynucleotides encoding the human **keratinocyte growth factor-2** (**KGF-2**, also known as fibroblast growth factor-12) and its variants, polypeptides encoded by such polynucleotides, the use of such polynucleotides and polypeptides, as well as the production of such polynucleotides and polypeptides. This invention further relates to the therapeutic use of **KGF-2** to promote or accelerate wound healing in a variety of associated diseases. This invention also relates to novel mutant forms of **KGF-2** that show enhanced activity, increased stability, higher yield, or better solubility The **KGF-2** precursor consists of 208 amino acid residues, with a signal moiety cleaved between residues Val35-Thr36 or Thr36-Cys37. N-terminal deletion mutants (from 38 to 137 residues removed from the N-terminus of the precursor protein) and C-terminal mutants (1 to 55 residues removed from the C-terminus), as well as substitution mutants (Cys37→Ser, Cys106→Ser, and residues 183, 188, 191, or 194) were also constructed. Site-specific mutagenesis and recombinant cloning procedures are provided.

RE.CNT 84 THERE ARE 84 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:250182 CAPLUS
DN 133:12799
TI **Keratinocyte growth factor-2**
AU Jimenez, Pablo A.; Greenwalt, Dale; Mendrick, Donna L.; Rampy, Mark A.; Su, Jeffrey; Leung, Kam H.; Connolly, Kevin M.
CS Human Genome Sciences, Inc., Rockville, MD, 20850, USA
SO New Cytokines as Potential Drugs (2000), 101-119. Editor(s): Narula, Satwant K.; Coffman, Robert. Publisher: Birkhaeuser Verlag, Basel, Switz. CODEN: 68URAB
DT Conference; General Review
LA English
AB A review, with 79 refs., on **keratinocyte growth factor-2** (**KGF-2**). The following topics were discussed: isolation and purification of **KGF-2** expressed in E. coli; **KGF-2** stimulation of keratinocyte proliferation in vitro; wound healing; as treatment for **inflammatory** bowel disease; its toxicity profile; and its pharmacokinetics.

RE.CNT 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:615028 CAPLUS
DN 131:282007
TI Efficacy of **keratinocyte growth factor-2** in dextran sulfate sodium-induced murine colitis
AU Miceli, Renee; Hubert, Melissa; Santiago, Gemma; Yao, Da-Lin; Coleman, Timothy A.; Huddleston, Kathleen A.; Connolly, Kevin
CS Dep. Pharmacol., Human Genome Sci., Inc., Rockville, ME, USA

SO Journal of Pharmacology and Experimental Therapeutics (1999), 290(1), 464-471
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB The purpose of this study was to determine the efficacy of a novel human protein, **keratinocyte growth factor-2** (**KGF-2**), in a model of murine colitis induced by ad libitum exposure to a 4% solution of dextran sulfate sodium (DSS) in the drinking water. Initial evaluation of **KGF-2** was based on its ability to reduce weight loss, stool score, and histol. score in mice exposed to DSS for 7 days. When **KGF-2** (0.1-10.0 mg/kg l.p. or s.c.) was injected daily into DSS-treated mice from day 0 to 7, it significantly reduced all three parameters in a dose-response fashion, with a min. ED of between 1 and 3 mg/kg. When **KGF-2** was given therapeutically, starting 4 days after initiation of the 7-day DSS treatment, the 3- but not the 0.5-mg/kg dose significantly enhanced weight recovery after discontinuation of DSS treatment. When DSS treatment was prolonged beyond the normal 7 days, therapeutic intervention on day 2 or 4 also significantly reduced mortality, weight loss, and school score at the 1- and 3-mg/kg dose. Therapeutic treatment also resulted in reduction of colon myeloperoxidase levels by ore than 50%. These expts. suggest that **KGF-2** may be clin. useful in the treatment of **inflammatory** bowel diseases such as ulcerative colitis and Crohn's disease.

L6 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:394356 CAPLUS
DN 129:62975
TI Use of keratinocyte growth factors and glucagon-like peptide 2 to increase proliferation and/or differentiation of epithelial cells of gastrointestinal tract
IN Farrell, Catherine L.; Li, Yue-Sheng
PA Amgen Inc., USA; Farrell, Catherine L.; Li, Yue-Sheng
SO PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9824813	A2	19980611	WO 1997-US22735	19971208
	WO 9824813	A3	19980806		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9856962	A1	19980629	AU 1998-56962	19971208
	EP 1012186	A2	20000628	EP 1997-953157	19971208
	EP 1012186	B1	20020717		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2001510333	T2	20010731	JP 1998-525894	19971208
	AT 220689	E	20020815	AT 1997-953157	19971208
	ES 2181054	T3	20030216	ES 1997-953157	19971208
	MX 9905163	A	20000228	MX 1999-5163	19990603
PRAI	US 1996-32533P	P	19961206		
	US 1997-62074P	P	19971015		
	WO 1997-US22735	W	19971208		

AB The combined use of KGF variants and GLP-2 to increase proliferation and/or differentiation of epithelial cells of gastrointestinal tract, especially to treat chemotherapy-related mucositis, is disclosed. The effects of **KGF** and GLP-**2** are synergistic.

L6 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:251269 CAPLUS
DN 128:304431
TI Recombinant production of **keratinocyte growth factor-2** variants and their therapeutic uses
IN Narhi, Linda Owens; Osslund, Timothy D.
PA Amgen Inc., USA; Narhi, Linda Owens; Osslund, Timothy D.
SO PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9816642	A1	19980423	WO 1997-US18607	19971015
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9747576	A1	19980511	AU 1997-47576	19971015
	AU 727678	B2	20001221		
	GB 2322132	A1	19980819	GB 1998-11279	19971015
	GB 2322132	B2	19990922		
	DE 19781038	T	19981210	DE 1997-19781038	19971015
	EP 935652	A1	19990818	EP 1997-910119	19971015
	EP 935652	B1	20040331		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2001506975	T2	20010529	JP 1998-518565	19971015
	MX 9903532	A	20000228	MX 1999-3532	19990415
	US 2004043924	A1	20040304	US 2003-665526	20030919
PRAI	US 1996-28493P	P	19961015		
	US 1996-32781P	P	19961206		
	US 1996-33046P	P	19961211		
	WO 1997-US18607	W	19971015		
	US 1999-284100	A1	19990407		

AB The present invention concerns variants and chemical derivs. of **keratinocyte growth factor-2** (**KGF-2**) protein. In particular, the recombinant production in Escherichia coli is provided for deletion derivs. of human **KGF -2** in which the N-terminal 32 or 21 amino acids are deleted, and for the substitution derivative in which Arg-149 is replaced by Gln. Also disclosed are nucleic acid mols. encoding such variants, as well as methods for using such variants and chemical derivs. to stimulate epithelial cell proliferation. **KGF-2** proteins are effective in treating chemotherapy-induced pulmonary fibrosis, radiation- and chemical-induced mucositis models, colitis, cirrhosis, hepatectomy, acute hepatotoxicity, diabetes, and hypoxia-induced lung injury.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:251069 CAPLUS
DN 128:317658

TI Uses of **keratinocyte growth factor-2**
IN Lacey, David L.; Ulich, Thomas R.; Danilenko, Dimitry M.; Farrell, Catherine L.
PA Amgen Inc., USA; Lacey, David L.; Ulich, Thomas R.; Danilenko, Dimitry M.; Farrell, Catherine L.
SO PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9816243	A1	19980423	WO 1997-US18667	19971015
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9850806	A1	19980511	AU 1998-50806	19971015
	AU 725509	B2	20001012		
	EP 941110	A1	19990915	EP 1997-913676	19971015
	EP 941110	B1	20040218		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2001506586	T2	20010522	JP 1998-518589	19971015
	AT 259651	E	20040315	AT 1997-913676	19971015
	MX 9903528	A	20000228	MX 1999-3528	19990415
	US 2003144202	A1	20030731	US 2002-314372	20021205
PRAI	US 1996-28495P	P	19961015		
	US 1996-32253P	P	19961206		
	US 1996-33457P	P	19961210		
	WO 1997-US18667	W	19971015		
	US 1999-284101	A1	19990407		

AB The present invention concerns the use of a **KGF-2** protein(s) as a therapeutic agent, suitably formulated in a pharmaceutical composition, for the specific treatment of disease states and medical conditions afflicting tissues and organs such as in the eye, ear, gums, pancreas, urinary bladder, liver and gastrointestinal tract.
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:126354 CAPLUS
DN 128:201362
TI Construction of deletion and substitution mutants of human **keratinocyte growth factor-2** and their use to promote wound healing
IN Duan, Roxanne; Ruben, Steven M.; Jimenez, Pablo; Rampy, Mark A.; Mendrick, Donna; Zhang, Jun; Ni, Jian; Moore, Paul A.; Coleman, Timothy A.; et al.
PA Human Genome Sciences, Inc., USA; Duan, Roxanne; Ruben, Steven M.; Jimenez, Pablo; Rampy, Mark A.; Mendrick, Donna; Zhang, Jun; Ni, Jian; Moore, Paul A.; Coleman, Timothy A.
SO PCT Int. Appl., 253 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9806844	A1	19980219	WO 1997-US14112	19970813
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,				

DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2430223	AA	19960822	CA 1995-2430223	19950214	
EP 1323824	A2	20030702	EP 2003-6708	19950214	
EP 1323824	A3	20040121			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE					
PT 815115	T	20031031	PT 1995-911700	19950214	
ES 2194049	T3	20031116	ES 1995-911700	19950214	
AU 9739770	A1	19980306	AU 1997-39770	19970813	
AU 739773	B2	20011018			
EP 950100	A1	19991020	EP 1997-937200	19970813	
EP 950100	B1	20040211			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
CN 1234071	A	19991103	CN 1997-197264	19970813	
NZ 333725	A	20001027	NZ 1997-333725	19970813	
JP 2000517174	T2	20001226	JP 1998-509953	19970813	
EP 1247530	A2	20021009	EP 2002-1059	19970813	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
EP 1247862	A2	20021009	EP 2002-1060	19970813	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
AT 259420	E	20040215	AT 1997-937200	19970813	
PRAI US 1996-23852P	P	19960813			
US 1997-39045P	P	19970228			
CA 1995-2210444	A3	19950214			
EP 1995-911700	A3	19950214			
EP 1997-937200	A3	19970813			
WO 1997-US14112	W	19970813			

AB This invention relates to newly identified polynucleotides encoding the human **keratinocyte growth factor-2** (**KGF-2**, also known as fibroblast growth factor-12) and its variants, polypeptides encoded by such polynucleotides, the use of such polynucleotides and polypeptides, as well as the production of such polynucleotides and polypeptides. This invention further relates to the therapeutic use of **KGF-2** to promote or accelerate wound healing in a variety of associated diseases. This invention also relates to novel mutant forms of **KGF-2** that show enhanced activity, increased stability, higher yield, or better solubility The **KGF-2** precursor consists of 208 amino acid residues, with a signal moiety cleaved between residues Val35-Thr36 or Thr36-Cys37. N-terminal deletion mutants (from 38 to 137 residues removed from the N-terminus of the precursor protein) and C-terminal mutants (1 to 55 residues removed from the C-terminus), as well as substitution mutants (Cys37→Ser, Cys106→Ser, and residues 183, 188, 191, or 194) were also constructed. Site-specific mutagenesis and recombinant cloning procedures are provided.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:49875 CAPLUS
DN 128:164458
TI Effects of keratinocyte growth factor on the proliferation and radiation survival of human squamous cell carcinoma cell lines in vitro and in vivo
AU Ning, Shoucheng; Shui, Chaoxiang; Khan, Waqqar B.; Benson, William; Lacey, David L.; Knox, Susan J.
CS Department of Radiation Oncology, Stanford University Medical Center,

Stanford, CA, 94305-5105, USA
SO International Journal of Radiation Oncology, Biology, Physics (1998), 40(1), 177-187
CODEN: IOBPD3; ISSN: 0360-3016
PB Elsevier Science Inc.
DT Journal
LA English
AB Keratinocyte growth factor (KGF) has potent mitogenic activity on normal epithelial cells and has been found to enhance intestinal crypt cell survival in irradiated mice and to prevent radiation and chemotherapy-induced mucositis in animal models. The purpose of the study reported here is to investigate the effect of recombinant human KGF on the proliferation and survival of human squamous carcinoma cell lines following irradiation The level of KGF receptor (KGFR) mRNA in normal Balb/Mk cell line and human head and neck squamous carcinoma cell lines was assessed using a RNase protection assay. The clonogenic assay and MTT assay were used to study the proliferative effects of KGF on human tumor cell lines and Balb/MK cell line in vitro. Effects of KGF on in vivo tumor growth and radiosensitivity were studied in three KGFR-pos. human squamous cell carcinoma xenografts (FaDu, Detroit 562 and A431) in nude mice, and a murine KGFR-neg. melanoma tumor (B16) in Balb/c mice. Seven of 10 tumor cell lines studied expressed KGFR mRNA. None of these tumor cell lines showed enhanced proliferation when exposed to **KGF** for 2 days or less. Prolonged exposure to KGF for 7 days or longer resulted in low level stimulation of proliferation in both clonogenic and MTT assays in four of seven KGFR-pos. cell lines. Two KGFR-neg. cell lines also had a low proliferative response to KGF in a clonogenic assay, but not in the MTT assay. Normal keratinocyte Balb/MK cells, which expressed a moderate level of KGFR mRNA, had a strongly proliferative response to KGF. Its KGF enhancement ratio (KER) of plating efficiency was 24-70 times higher than that of the tumor cells studied ($p < 0.001$). The KGF-stimulated tumor cell growth was almost completely inhibited by heparin or epidermal growth factor (EGF). There were no significant differences ($p > 0.05$) in the survival of any of tumor cell lines in the presence or absence of KGF (100 ng/mL) irradiated with doses of 0-15 Gy, and no significant differences ($p > 0.05$) between the radiobiol. parameters D0, Dq, and n number from the SHMT model, α, β, and α/β ratio from the LQ model and SF2 for radiation survival curves for cell lines irradiated in the presence or absence of KGF. Three KGFR-pos. human squamous cell carcinoma xenografts in nude mice, and a murine KGFR-neg. melanoma tumor in Balb/c mice treated with 1.0 mg/kg of KGF for 3 days grew at the same rate as in untreated mice. The recombinant human KGF resulted in little or no stimulation of the proliferation of human head and neck squamous tumor cell lines and did not affect the radiosensitivity of these cell lines in vitro and in vivo. Therefore, KGF may be of clin. value in preventing radiation-induced mucositis and may have the potential to increase the therapeutic index of radiotherapy for treatment of cancers